

Supplementary Material

Table of Contents

Table 1: Studies included and study characteristics	Page 2
Table 2: Studies excluded	Page 20
References for the two table	Page 22
Supplementary Figures 1 – 8: Forest plots of most significant SNPs	Page 36
Supplementary Figures 9 – 15: Significant subgroup analyses	Page 44
Supplementary Figures 16 – 20: Sensitivity analyses forest plots	Page 51
Details of data from our lab	Page 56
Previous meta-analyses	Page 57
References	Page 58

Table 1: Studies included and study characteristics

Gene	Study	Ancestry	Type of study	Sample size	SNPs included in the study	Diagnosis criteria						Hardy Weinberg Equilibrium	Notes
						AD OS	AD OS -G	A D I-R	CA RS	DS M-IV	DS M III-R		
MTHFR	Park et al., 2014 ¹	Korean	Case Control	251 cases, 425 controls	rs1801133					X		Yes	
	Liu et al., 2011 ²	Caucasian	Case Control	512 cases, 384 controls	rs1801133, rs1801131	X		X		X		Yes	Includes a proband from 205 simplex families and a random proband from 307 multiple x families
	Guo et al., 2012 ³	Chinese (Han)	Case Control	186 cases, 186 controls	rs1801133							Yes	
	dos Santos et al., 2010 ⁴	European derived (Brazil)	Case Control	151 cases, 100 controls	rs1801133			X				Yes	

	James et al., 2006 ⁵	Caucasian (97%)	Case Control	356 cases, 205 controls	rs1801133, rs1801131	X			X	X		Yes	
	Pasca et al., 2009 ⁶	Caucasian (Romanian)	Case Control	39 cases, 80 controls	rs1801133					X		Yes	
	Mohammad et al., 2009 ⁷	Indian	Case Control	138 cases, 138 controls	rs1801133					X		Yes	
	Divyakolu et al., 2013 ⁸	Indian	Case Control	50 cases, 50 controls	rs1801133							HWE not given, manually checked (Yes)	
	Boris et al., 2004 ⁹	Caucasian	Case Control	168 cases, 5389 controls	rs1801133, rs1801131					X		Yes	
	Schmidt et al., 2011 ¹⁰	Mixed	Case Control	429 cases, 278 controls	rs1801133	X		X				Yes	
EN2	Gharani et al., 2004 ¹¹	Caucasian (AGRE sample)	Family based	167 families	rs1861972, rs1861973, rs3735653			X				Yes	
	Yang et al., 2010 ¹²	Chinese (Han)	Case Control	193 cases, 309 controls	rs1861972, rs1861973					X		Yes	
	Sen et al., 2010 ¹³	Indian	Family based	128 families of ASD children	rs1861973, rs3735653					X		Yes	

				comprising of 105 trios and 23 duos									
	Yang et al., 2008 ¹⁴	Chinese (Han)	Case Control	184 cases, 634 controls	rs1861972, rs1861973					X		Yes	Controls made of two groups, both the groups were combined in the analysis
	Prandini et al., 2008 ¹⁵	Italian	Family based	227 families	rs1861972						X		
	Benayed et al., 2005 ¹⁶	Caucasian (AGRE sample)	Family based	518 families	rs1861972, rs1861973			X				Yes	
	Warrier et al., 2014	Caucasian	Case Control	118 cases, 412 controls	rs1861972					X		Yes	
	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs1861972, rs3735653					X		Yes	
	Zhong et al., 2003 ¹⁸	Caucasian (AGRE sample)	Family based	204 families	rs3735653			X			X	Yes	

GRIK2	Jamain et al., 2002 ¹⁹	European and American	Family based	107 trios	rs2227281, rs2227283			X		X		Yes	
	Dutta et al., 2007 ²⁰	Indian	Family based	101 probands, 180 parents	rs2227281, rs2227283			X	X	X		Yes	
	Shuang et al., 2004 ²¹	Chinese (Han)	Family based	174 families	rs2227281, rs2227283					X			
	Kim et al., 2007 ²²	Korean	Family based	126 trios	rs2227281, rs2227283	X		X		X		Yes	
COMT	Limprasert et al., 2014 ²³	Thai	Family based	188 cases, 250 controls	Val158Met (rs4680)					X		Yes	Only Case-Control data used
	James et al., 2006 ⁵	Mixed	Case Control	360 cases and 205 controls	Val158Met (rs4680)			X	X	X		Yes	
	Guo et al., 2013 ²⁴	Chinese Han	Case Control	186 cases, 186 controls	Val158Met (rs4680)				X	X		Yes	
	Karam et al., 2013 ²⁵	Egyptian	Case Control	80 cases, 100 controls	Val158Met (rs4680)				X	X		Yes	

	Yirmiya et al., 2001 ²⁶	N.A.	Family based	35 families	Val158Met (rs4680)			X		X	X	Yes	This study used haplotype relative risk and as a result, the data was treated as a case-control study
TPH2	Coon et al., 2005 ²⁷	Mixed (Caucasian)	Case Control	88 cases, 95 controls	rs11179000	X		X				HWE not given, manually checked (Yes)	
	Ramoz et al., 2006 ²⁸	Mixed	Family based	352 families	rs11179000			X				Yes	
	Singh et al., 2013 ²⁹	Indian	Case Control	136 cases, 165 controls	rs11179000					X		Yes	
MACROD2	Curran et al., 2011 ³⁰	Mixed	Case Control	1170 cases, 35307 controls	rs4141463			X		X		Yes	

	Prandini et al., 2008 ¹⁵	Italian	Family based	227 families	rs4141463						X	Yes	
	Anney et al., 2010 ³¹	Mixed	Family based	1158 families	rs4141463	X		X				Yes	
DRD3	Krom et al., 2009 ³²	Dutch	Case Control	254 cases, 404 controls	rs167771					X		Yes	
	Toma et al., 2013 ³³	Spanish	Case Control	326 cases, 350 controls	rs167771					X		Yes	
HTR2 A	Veenstra-VanderWeele et al., 2002 ³⁴	Caucasian, African American, Asian American, Hispanic	Family based	115 trios	rs6311, rs6314					X		NA	
	Guhathakurta et al., 2009 ³⁵	Indian	Family based and Case Control	97 trios	rs6311, rs6314					X		Yes	Only Family based data used
	Hranilovic et al., 2010 ³⁶	Croatian	Case Control	103 cases, 214 controls	rs6311, rs6314					X		Yes	
	Cho et al., 2007 ³⁷	Korean	Family based	26 trios	rs6311				X			Yes	
	Smith et al., 2014 ³⁸	Mixed	family based	158 trios	rs6311, rs6314	X				X		N.A.	
	Nyffeler et al., 2014 ³⁹	Caucasian	Case Control	76 cases 99 controls	rs6311	X		X				Yes	

STX1A	Durdiaková et al., 2014 ⁴⁰	Caucasian	Family based	479 cases, 650 controls	rs4717806, rs6951030					X		Yes	
	Nakamura et al., 2011 ⁴¹	Japanese	Family based	378 individuals	rs4717806, rs6951030			X		DS M-IV-TR		Yes	
	Nakamura et al., 2008 ⁴²	Caucasian	Family based	249 trios	rs4717806, rs6951030	X		X				Yes	
	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs4717806, rs6951030					X		Yes	
BDNF	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs6265					X		Yes	
	Cheng et al., 2009 ⁴³	Chinese	Case Control	174 cases, 349 controls	rs6265			X	X	X		Yes	
	Nishimura et al., 2007 ⁴⁴	AGRE	Family based	104 trios	rs6265					X		Yes	
ITGB3	Singh et al., 2013 ²⁹	Indian	Case Control	139 cases, 165 controls	rs5918				X	X		Yes	
	Cochrane et al., 2010 ⁴⁵	Irish	Family based	177 trios	rs5918		X	X				Yes	
	Coutinho et al., 2007 ⁴⁶	Portugese	Family based	186 trios	rs5918			X	X	X		NA	
CNTN AP2	Sampath et al., 2013 ⁴⁷	Mixed	Family based	2051 families	rs7794745, rs2710102	X		X				Yes	
	Toma et al., 2013 ⁴⁸	Spanish	Case Control	322 cases, 524 controls	rs7794745, rs2710102					X		Yes	

	Li et al., 2010 ⁴⁹	Chinese	Family based	322 individual s	rs7794745					X		NA	
RELN	Sharma et al., 2013 ⁵⁰	South African	Case Control	136 cases, 208 controls	rs736707, rs362691					X		Yes	
	Fu et al., 2013 ⁵¹	Chinese (Han)	Case Control	205 cases, 210 controls	rs2073559					X		Yes	
	He et al., 2011 ⁵²	Chinese (Han)	Family based, Case Control	232 cases, 283 controls	rs736707, rs362691, rs2073559					X		NA	
	Dutta et al., 2008 ⁵³	Indian	Family based, Case Control	102 cases, 283 controls	rs362691				X	X		Yes	
	Li et al., 2008 ⁵⁴	Chinese (Han)	Case Control	213 cases, 160 controls	rs736707, rs362691					X		Yes	
	Bonora et al., 2003 ⁵⁵	Mixed	Family based	342 cases, 194 controls	rs362691, GGC repeat	X		X				NA	
	Serajee et al., 2006 ⁵⁶	Mixed	Family based	174 cases, 349 controls	rs736707, rs362691			X				Yes	
	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs736707					X		Yes	
	Warrier et al., 2014	Caucasian	Case Control	118 cases, 412 controls	rs736707							Yes	

	Persico et al., 2001 ⁵⁷	American/Italian	Family based and Case Control	95 cases, 186 controls	GGC repeat					X		Yes	
	Krebs et al., 2002 ⁵⁸	Mixed	Family based	167 families	GGC repeat			X		X		NA	
	Zhang et al., 2002 ⁵⁹	Canada	Case Control	126 cases, 347 controls	GGC repeat	X		X				Yes	
	Li et al., 2004 ⁶⁰	Mixed	Family based	107 families	GGC repeat	X		X				NA	
	Ashley-Koch et al., 2007 ¹⁴⁴	Caucasian	Family based	470	rs2073559					X		Yes	
	Dutta et al., 2007 ⁶¹	Indian	Family based/Case Control	55 cases, 80 controls	rs736707, GGC repeat				X	X		Yes	
SLC25A12	Ramoz et al., 2004 ⁶²	Egyptian	Family based	2000 (710,1280)	rs2056202	X				X		NA	
	Segurado et al., 2005 ⁶³	Irish	Family based	158 trios	rs2292813, rs2056202					X		NA	
	Blasi et al., 2006 ⁶⁴	Caucasian	Family based/Case Control	531 individuals (261, 174)	rs2056202					X		NA	
	Chien et al., 2010 ⁶⁵	Chinese (Han)	Case Control	465 cases, 450 controls	rs2056202, rs2292813	X				X		Yes	
	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs2056202					X		Yes	

	Correia et al., 2006 ⁶⁶	Italian	Case Control	NA	rs2056202			X		X		Yes	
	Palmieri et al., 2010 ⁶⁷	Caucasian	Family based	197 families	rs2056202, rs2292813							NA	
	Ramoz et al., 2008 ⁶⁸	AJMGB	Family based	334 families	rs2292813	X				X		NA	
	Durdiakova et al., 2014 ⁶⁹	Caucasian	Case Control	117 cases, 412 controls	rs2056202					X		Yes	
PON1	Pasca et al., 2010 ⁷⁰	Romanian s	Case Control	50 cases, 85 controls	rs662, rs854560					X		Yes	
	D'Amelio et al., 2005 ⁷¹	American caucasian/Italians	Case Control/Family based	177 cases, 180 controls (Italians), 107 cases, 376 controls (Americans)	rs662, rs854560	X		X		X		Yes	Only Case Control data used
ASMT	Melke et al., 2008 ⁷²	Caucasian	Case Control	278 cases, 255 controls	rs4446909, rs5989681			X		X		Yes	
	Toma et al., 2007 ⁷³	Finnish, Italian and European (IMGSAC)	Case Control	127 cases, 100 controls (Finnish), 69 cases, 90 controls (Italian),	rs4446909, rs5989681, rs6644635	X		X		X		Yes	

				194 cases, 192 controls (European - IMGSAC)									
	Wang et al., 2013 ⁷⁴	Chinese	Case Control	398 cases, 437 controls	rs4446909, rs5989 681, rs6644635				X	X	AB C	Yes	
ADA	Hettinger et al., 2008 ⁷⁵	NA	Case Control	125 cases, 167 controls	rs7359837	X		X				Yes	
	Bottini et al., 2001 ⁷⁶	Italian	Case Control	118 cases, 126 controls	rs7359837					X		Yes	
	Persico et al., 2000 ⁷⁷	Italian	Case Control and Family based	91 cases, 152 controls	rs7359837					X		Yes	
SHAN K3	Sykes et al., 2009 ⁷⁸	NA (IMGSAC cohort)	Family based and case- pseudocon trol	308 families	rs9616915		X					Yes	Case- pseudoc ontrol data was used for analysis
	Shao et al., 2014 ⁷⁹	Chinese	Case Control	212 cases, 636 controls	rs9616915					X		Yes	

	Waga et al., 2011 ⁸⁰	Japanese	Case Control	128 cases, 228 controls	rs9616915					X		HWE not given, manually checked (Yes)	
MAOA	Verma et al., 2014 ⁸¹	Indian	Case Control	194 cases, 227 controls	uvntr				X	X		Yes	
	Salem et al., 2013 ⁸²	Egyptian	Case Control	53 cases, 30 controls	uvntr				X			Yes	
	Tassone et al., 2011 ⁸³	NA	Case Control	189 cases, 167 controls	uvntr	X		X				Yes	
NF1	Marui et al., 2004 ⁸⁴	Japanese	Case Control	74 cases, 122 controls	GxAlu -8 vs non-8 and 9 vs non-9					X		Yes	
	Mbarek et al., 1999 ⁸⁵	NA	Case Control	85 cases, 90 controls	GxAlu -8 vs non-8 and 9 vs non-9					X		Yes	
	Plank et al., 2001 ⁸⁶	Caucasian & African	Case Control	204 cases, 200 controls	GxAlu -8 vs non-8 and 9 vs non-9					X		Yes	
MET	Campbell et al., 2006 ⁸⁷	Italian	Family based and Case Control	702 cases, 189 controls	rs1858830					X		Yes	Only Case Control data used

	Jackson et al., 2009 ⁸⁸	South Carolina & Italian	Case Control	174 cases, 369 controls (South Carolina), 65 cases, 126 controls (Italian)	rs1858830	X		X	X			Yes	
	Sousa et al., 2009 ⁸⁹	Caucasian & Italian	TDT	1621 caucasian, 84 italian trios	rs1858830, rs38845					X		Yes	
	Campbell et al., 2008 ⁹⁰	Mixed, largely Caucasian	Case Control	629 cases, 312 controls	rs1858830					X		Yes	
	Thanseem et al., 2010 ⁹¹	Japanese	Family based	378 families	rs1858830, rs38845			X		X		Yes	
	Zhou et al., 2011 ⁹²	Chinese	Case Control	405 cases, 594 controls	rs1858830, rs38845				X	X		Yes	
GLO1	Wu et al., 2008 ⁹³	Chinese	Case Control	272 cases, 310 controls	rs2736654			X		X		Yes	
	Junaid et al., 2004 ⁹⁴	Multi	Case Control	71 cases, 49 controls	rs2736654			X				Yes	
	Kovač et al., 2014 ⁹⁵	Slovenian	Case Control	143 cases, 150 controls	rs2736654					X		Yes	

	Sacco et al., 2007 ⁹⁶	Italian, Caucasian-American	Case Control	371 cases, 171 controls	rs2736654	X		X		X		Yes	
OXTR	Liu et al., 2010 ⁹⁷	Japanese	Case Control	282 cases, 440 controls	rs2301261, rs2254298, rs2268495, rs2268491, rs237885, rs237887, rs53576, rs1042778, rs2268493					X		Yes	
	Jacob et al., 2007 ⁹⁸	Caucasian	Family based	57 trios	rs2254298,rs53576	X		X		X		Yes	
	Tansey et al., 2010 ⁹⁹	Caucasian	Family based	458 families	rs2268494, rs237894, rs2268495, rs2268490, rs2268491, rs237885, rs237887, rs1042778					X		NA	
	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs2301261, rs2254298, rs237894, rs2268490, rs237885, rs53576, rs2268493					X		Yes	
	Nyffeler et al., 2014 ³⁹	Caucasian	Case Control	76 cases 99 controls	rs2268494, rs2301261, rs2254298, rs53576	X		X				Yes	

	DiNapoli et al., 2014 ¹⁰⁰	Caucasian	Case Control	118 cases, 412 controls	rs2301261, rs2254298, rs237894, rs2268490, rs237885, rs53576, rs2268493					X		Yes	
OMG	Vourc'h P et al., 2003 ¹⁰¹	Caucasian	Case Control	65 cases, 101 controls	rs11080149					X		Yes	
	Martin et al., 2007 ¹⁰²	US, Canada, Italian	Family based	431 families	rs11080149		X	X		X		Yes	
HOXA 1	Chakrabarti et al., 2009 ¹⁷	Caucasian	Case Control	174 cases, 349 controls	rs10951154					X		Yes	
	Devlin et al., 2002 ¹⁰³	Mixed	Family based	231 families	rs10951154	X		X		X		NA	

	Collins et al., 2003 ¹⁰⁴	Mixed	Case Controls and Family based	204 cases, 159 controls in total; 187 families	rs10951154					X		Yes (Caucasian), No (African American)	We used Case Control for the caucasian population and Family based for the African-american population
	Conciatori et al., 2004 ¹⁰⁵	Italian and Caucasian	Case Control and Family based	127 cases, 174 controls	rs10951154					X		No	Only Family based data used
	Sen et al., 2007 ¹⁰⁶	Indian (Northern and Eastern)	Case Control	80 cases, 149 controls	rs10951154				X	X		Yes	
	Gallagher et al., 2004 ¹⁰⁷	Irish	Family based	78 families	rs10951154	X		X				NA	

	Romano et al., 2003 ¹⁰⁸	Italian	Family based and Case Control	85 cases, 132 controls	rs10951154					X		Yes	Only Case Control data used
	Talebizadeh et al., 2002 ¹⁰⁹	Mixed	Case Control	35 cases, 35 controls	rs10951154				X	X		Yes	
	Li et al., 2002 ¹¹⁰	NA	Family based	110 multiplex	rs10951154	X		X				Yes	
	Ingram et al., 2000 ¹¹¹	Caucasian	Family based and Case Control	50 families	rs10951154					X		NA	
SLC6A4	Ramoz et al., 2006 ¹¹²	AGRE	Family based	352 families	5-HTTLPR, rs2020936, rs2020942			X				NA	
	Devlin et al., 2005 ¹¹³	NIH	Family based	390 families	5-HTTLPR, rs2020936			X		X		Yes	
	Kim et al., 2002 ¹¹⁴	Caucasian	Family based	115 trios	5-HTTLPR, VNTR	X		X		X		Yes	
	Cho et al., 2007 ³⁷	Korean	Family based	126 trios	5-HTTLPR					X		Yes	
	Klauck et al., 1997 ¹¹⁵	Caucasian (One family: Asian)	Family based	65 trios	5-HTTLPR, VNTR	X		X		X		NA	
	Cook et al., 1997 ¹¹⁶	Caucasian, African-American, Hispanic-	Family based	86 families	5-HTTLPR, VNTR	X		X				NA	

		American, Asian- American											
	Conroy et al., 2004 ¹¹⁷	Irish	Family based	84 trios	5-HTTLPR, VNTR		X	X				Yes	
	Maestrini et al., 1999 ¹¹⁸	Caucasian	Family based	90 families	5-HTTLPR, VNTR		X					NA	
	Persico et al., 2000 ¹¹⁹	Italian/American	Family based	54 trios, 44 trios	5-HTTLPR					X		Yes	
	Tordjman et al., 2001 ¹²⁰	Caucasian	Family based	71 trios	5-HTTLPR							NA	
	Yirmiya et al., 2001 ²⁶	Isreal	Family based	34 families	5-HTTLPR			X		X	X	NA	
	Betancur et al., 2002 ¹²¹	Caucasian (Austria, Belgium, France, Italy, Norway, Sweden and United states)	Family based	53 families with 43 trios	5-HTTLPR, VNTR			X		X		NA	
	Coutinho et al., 2006 ⁴⁶	Portugese	Family based	196 families	5-HTTLPR, VNTR			X	X	X		NA	
	Mulder et al., 2005 ¹²²	Dutch	Family based	125 trios	5-HTTLPR, VNTR							NA	
	Koishi et al., 2006 ¹²³	Japanese	Family based	104 trios	5-HTTLPR					X		Yes	
	Guhathakurta et al., 2006 ¹²⁴	Indian	Family based	93 families	5-HTTLPR				X	X		Yes	
	Wu et al., 2005 ¹²⁵	Chinese	Family based	175 trios	rs2020936, rs2020942			X		X		Yes	

	Yoo et al., 2009 ¹²⁶	Korean	Family based	151 trios	rs2020936, rs2020942							Yes	
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Table 2: Studies excluded

Study	Reason for exclusion	Article name
Alarcon et al. 2008 ¹²⁷	Sample overlaps with Sampath <i>et al.</i> 2013	Linkage, association, and gene-expression analyses identify CNTNAP2 as an autism-susceptibility gene.
Anderson et al. 2008 ¹²⁸	Insufficient data	Examination of association to autism of common genetic variation in genes related to dopamine.
Cheng et al. 2009 ¹²⁹	Article inaccessible	Polyacrylamide gel-based microarray: a novel method applied to the association Study between the polymorphisms of BDNF gene and autism.
Egawa et al. 2012 ¹³⁰	Minor allele frequency is 0	A detailed association analysis between the tryptophan hydroxylase 2 (TPH2) gene and autism spectrum disorders in a Japanese population.
Gaita et al. 2010 ¹³¹	Sample overlaps with D'amelio 2005	Decreased serum arylesterase activity in autism spectrum disorders
Hutcheson et al., 2004 ¹³²	Insufficient data	Examination of NRCAM, LRRN3, KIAA0716, and LAMB1 as autism candidate genes
Kelemenova et al. 2010 ¹³³	Insufficient data	Polymorphisms of candidate genes in Slovak autistic patients.
Mei et al. 2007 ¹³⁴	Covariates used in analysis	Multifactor dimensionality reduction-phenomics: a novel method to capture genetic heterogeneity with use of phenotypic variables.
Petit et al. 1995 ¹³⁵	Insufficient data	Association study with two markers of a human homeogene in infantile autism.
Rabionet et al. 2006 ¹³⁶	Insufficient data	Lack of association between autism and SLC25A12.
Rehnstrom et al. 2007 ¹³⁷	Insufficient data	No association between common variants in glyoxalase 1 and autism spectrum disorders
Serajee et al. 2004 ¹³⁸	Sample overlaps with D'amelio 2005	Polymorphisms in xenobiotic metabolism genes and autism

Veatch et al. 2014 ¹³⁹	Sample overlaps with Toma 2007, Melke 2008 and Wang 2013. Further tests specifically individuals with sleep issues.	Genetic Variation in Melatonin Pathway Enzymes in Children with Autism Spectrum Disorder and Comorbid Sleep Onset Delay
Weiss et al. 2006 ¹⁴⁰	Tests for interaction	ITGB3 shows genetic and expression interaction with SLC6A4.
Xu et al. 2013 ¹⁴¹	Article inaccessible	Genetic polymorphisms of SNP loci in the 5' and 3' region of TPH2 gene in Northern Chinese Han population
McCauley et al., 2003 ¹⁴²	Sample overlaps with Ramoz et al., 2006	Linkage and association analysis at the serotonin transporter (SLC6A4) locus in a rigid-compulsive subset of autism
Yu et al. 2004	Article inaccessible and not traceable	Association study between HOXA1 A218G polymorphism and autism.
Arking et al., 2008 ¹⁴³	Sample overlaps with Sampath et al. 2013	A common genetic variant in the neurexin superfamily member CNTNAP2 increases familial risk of autism.

Studies mentioned in the table are studies that otherwise satisfy the inclusion criteria as mentioned in the Methods section. Several other studies were excluded as they did not meet all the criteria mentioned in the Methods section. These studies have not been listed in the table above.

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Supplementary Figures 1 – 8: Forest plots of most significant SNPs

Figure 1: Forest plot for rs7794745 (*CNTNAP2*)

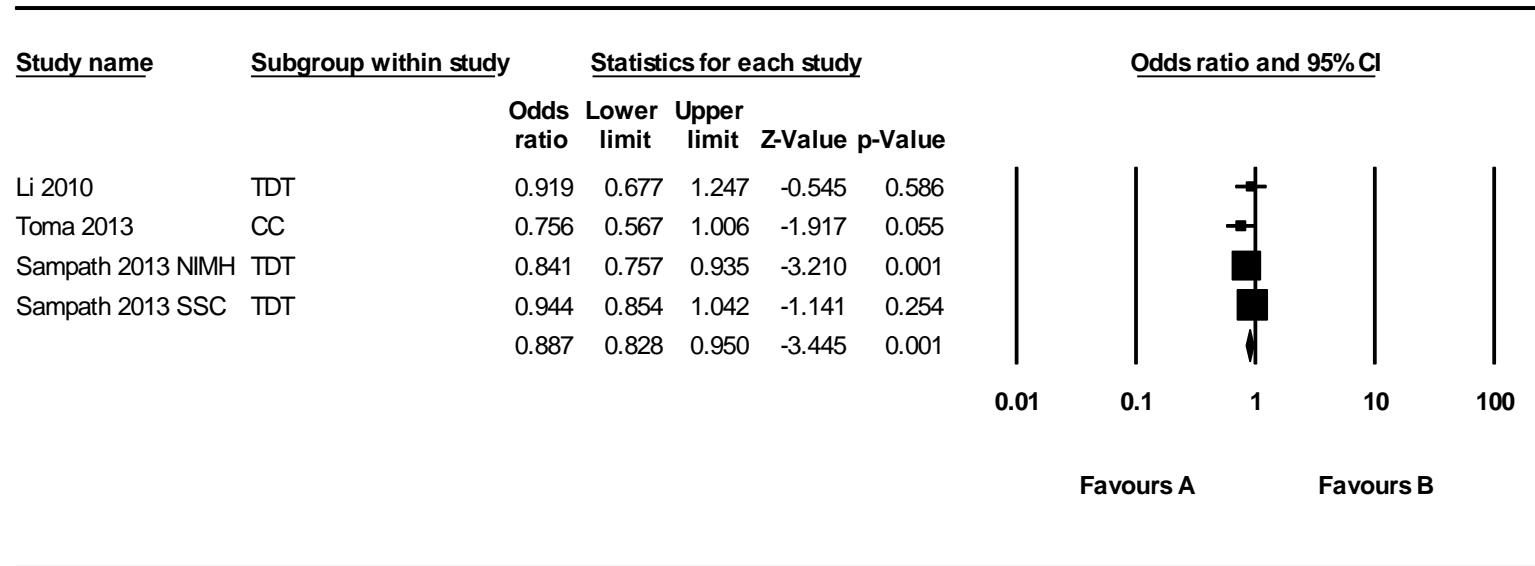


Figure 2: Forest plot for rs167771 (*DRD3*)

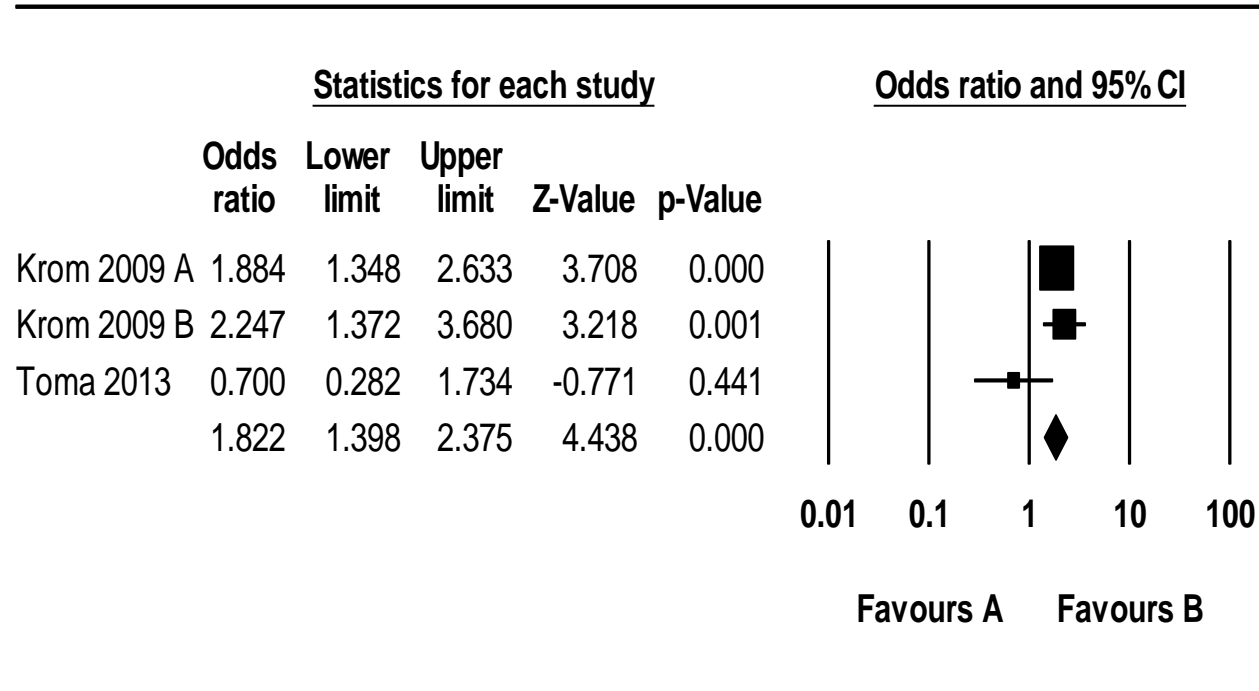


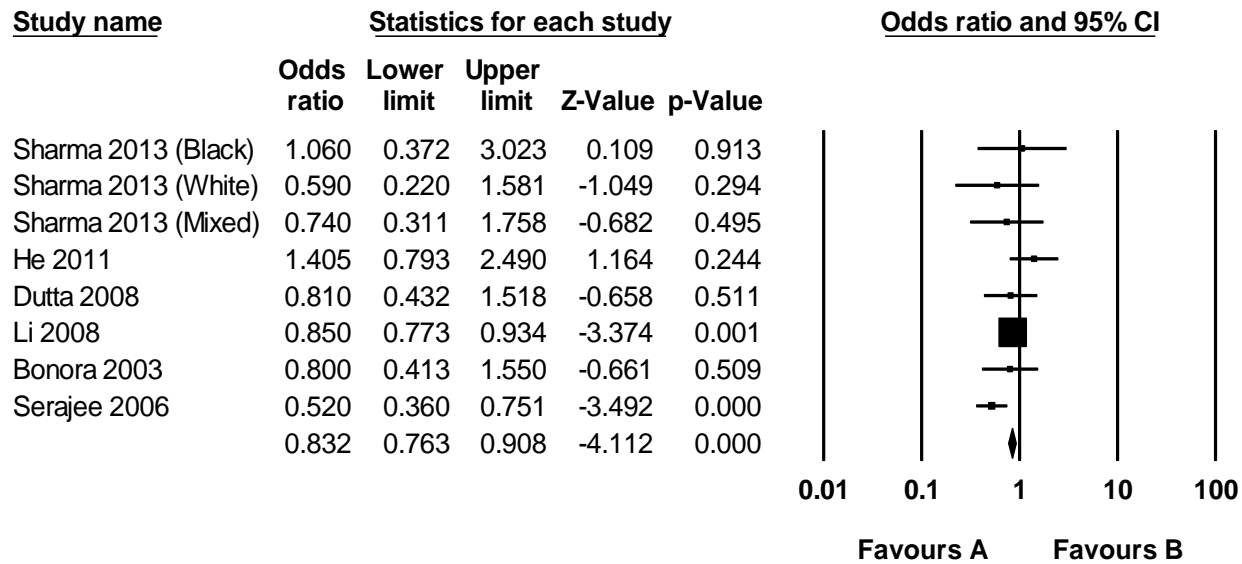
Figure 3: Forest plot for rs362691 (*RELN*)

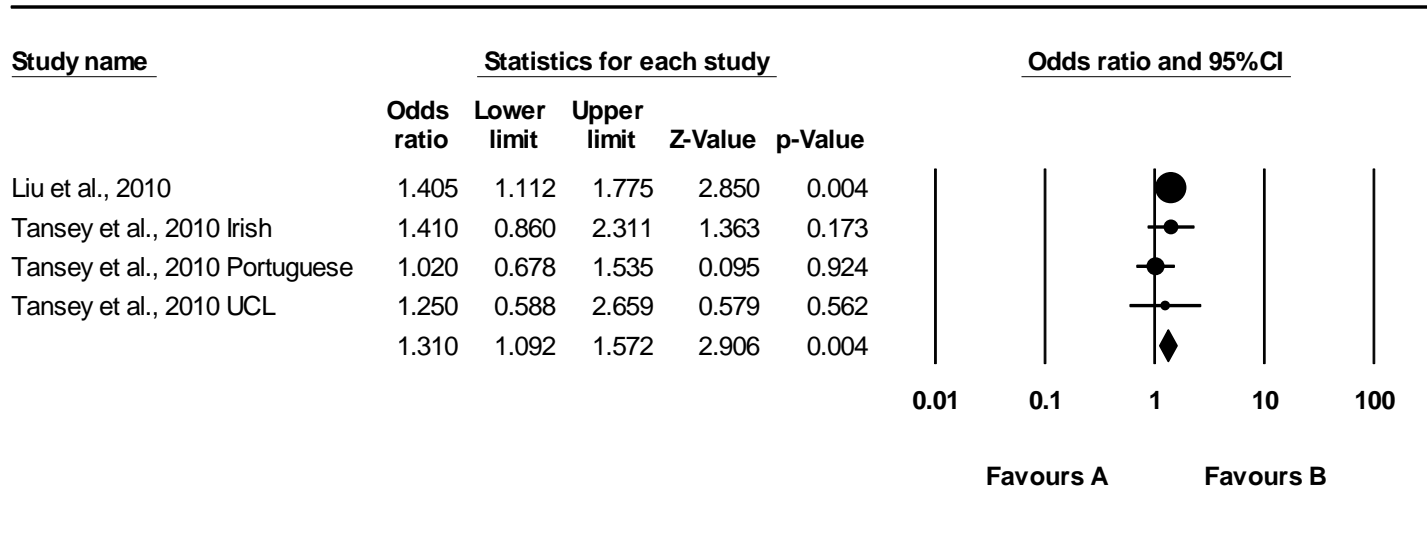
Figure 4: Forest plot for rs2268491 (*OXTR*)

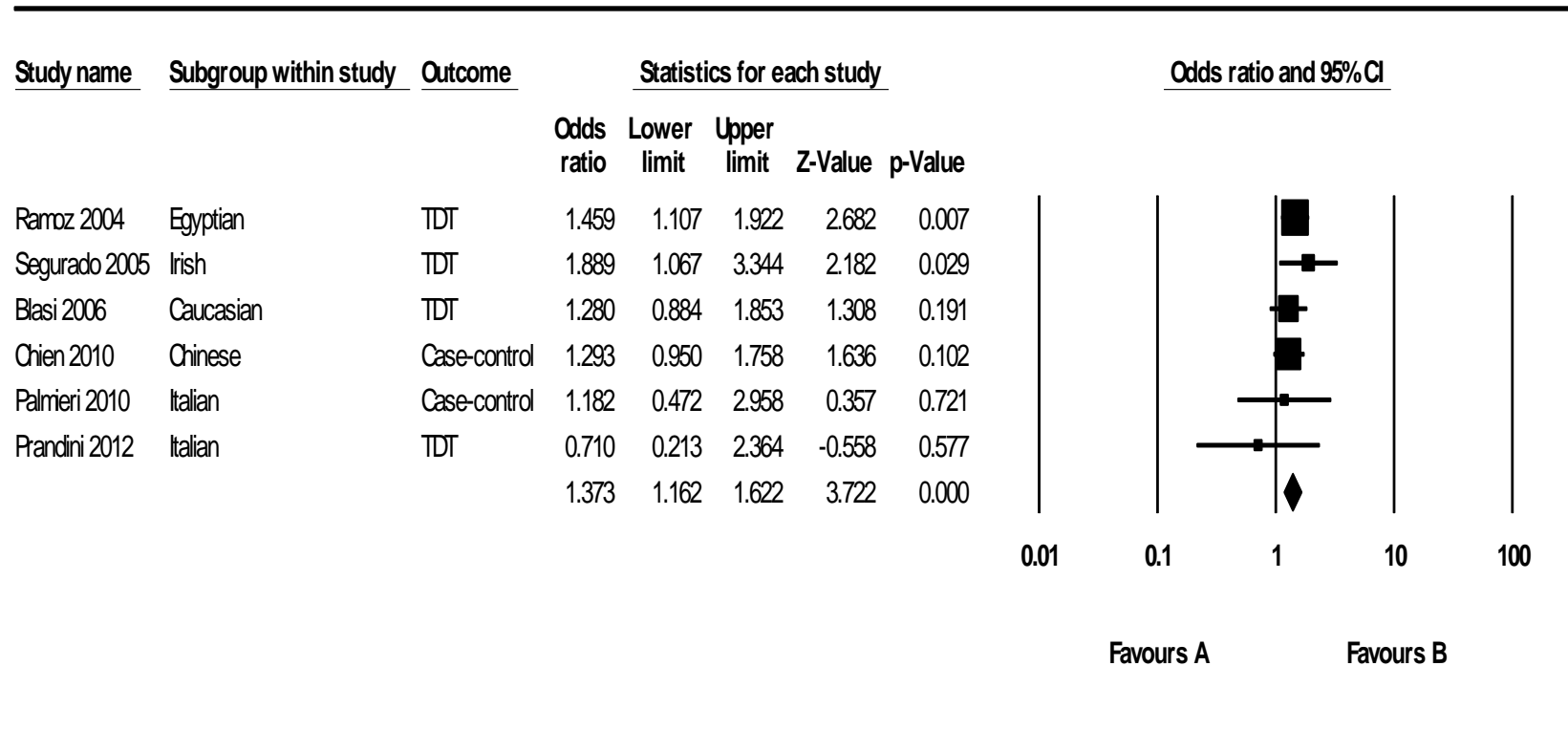
Figure 5: Forest plot for rs2292813 (*SLC25A12*)

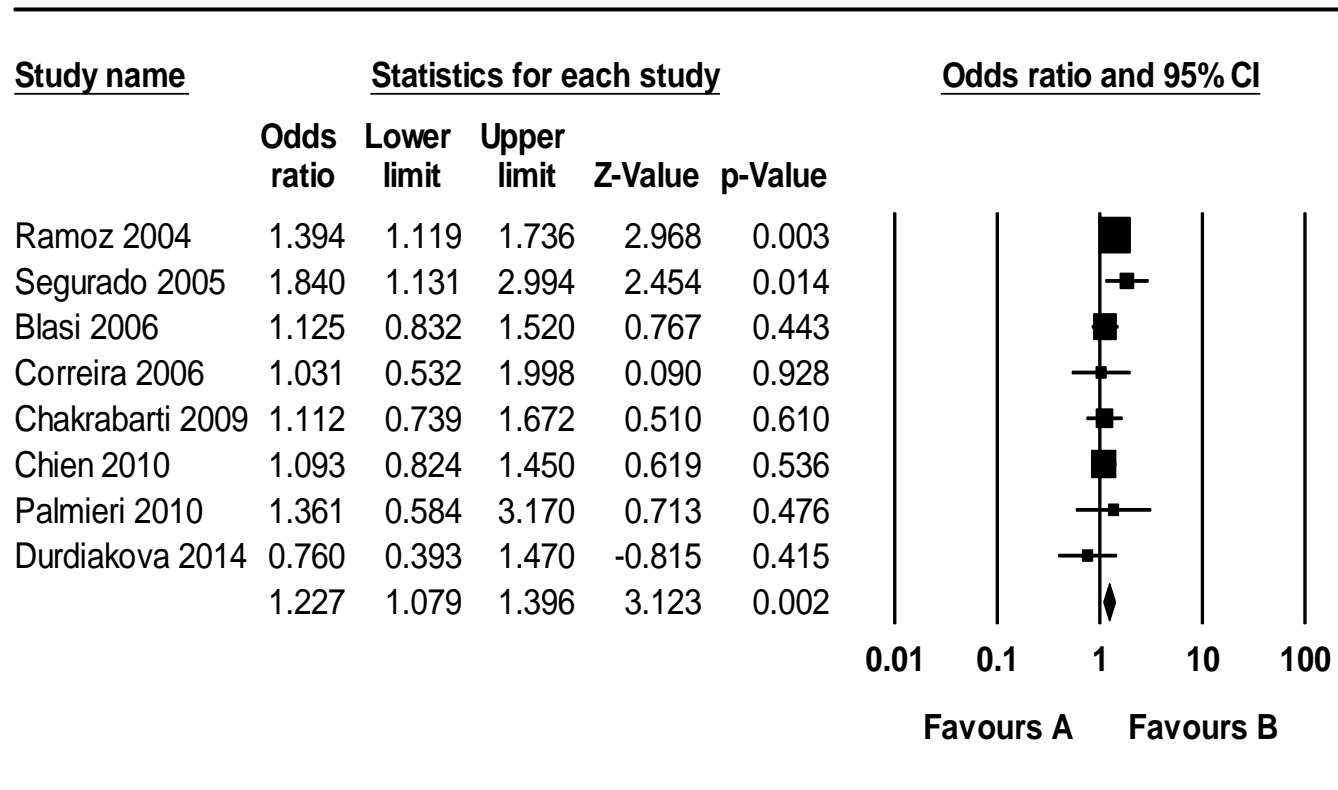
Figure 6: Forest plot for rs2056202 (*SLC25A12*)

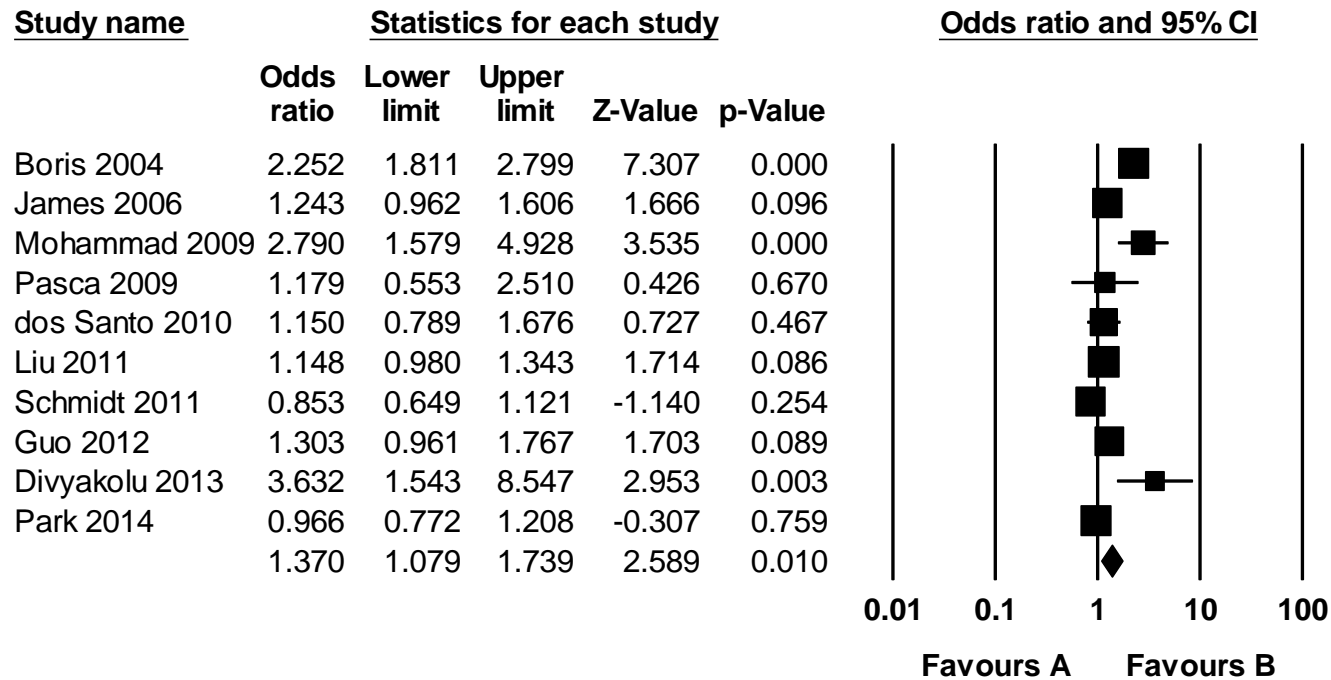
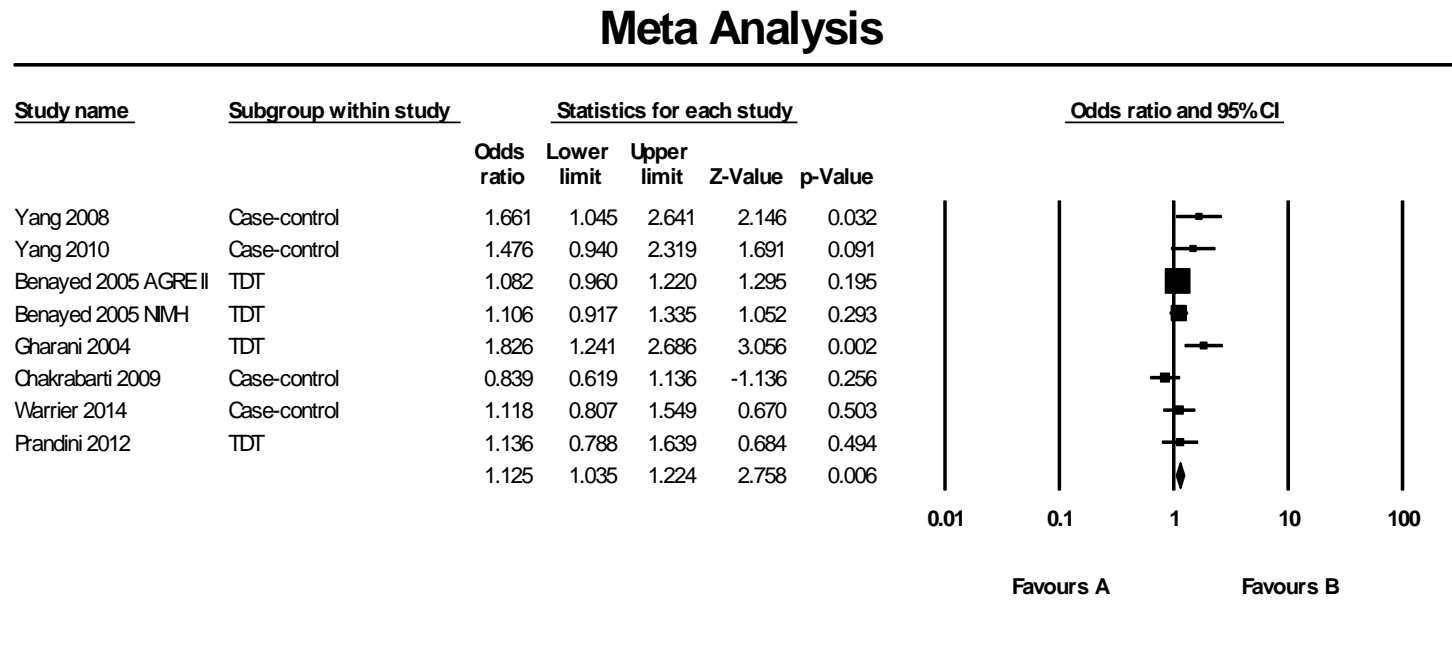
Figure 7: Forest plot for rs1801133 (*MTHFR*)

Figure 8: Forest plot for rs1861972 (EN2)



Supplementary Figures 9 – 15: Significant subgroup analyses

Figure 9: STin2 VNTR (*SLC6A4*), Caucasian only

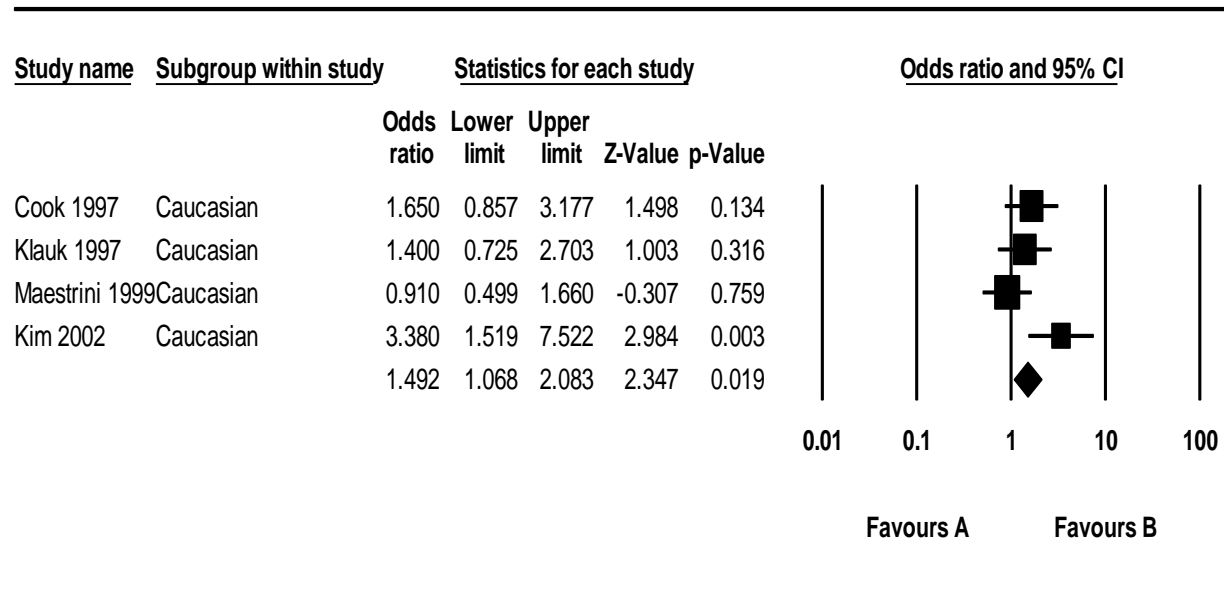


Figure 10: rs362691 (*RELN*), Case-control only

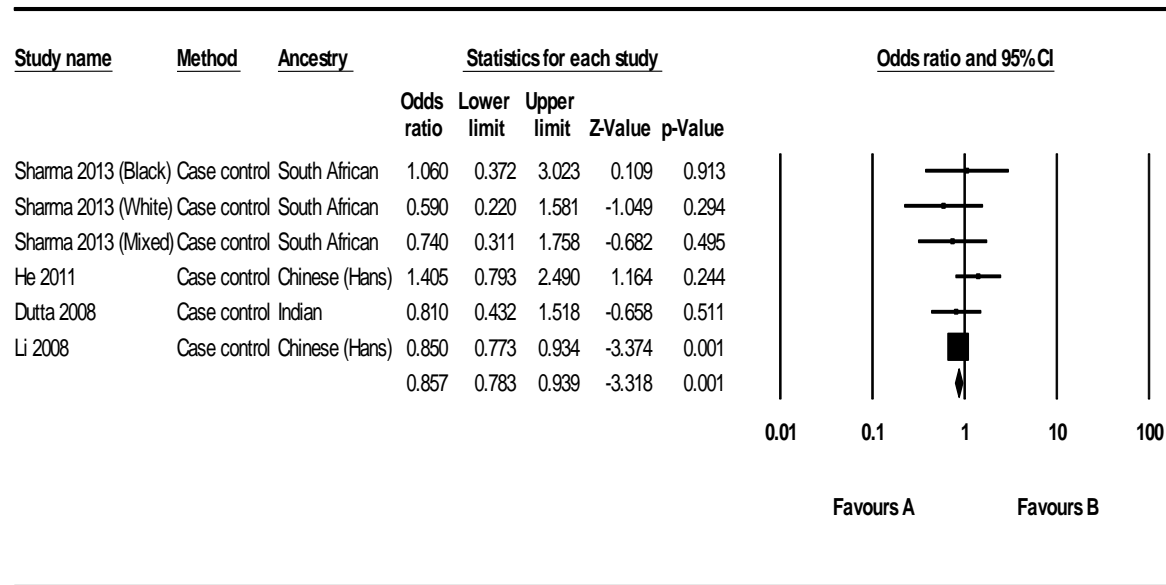


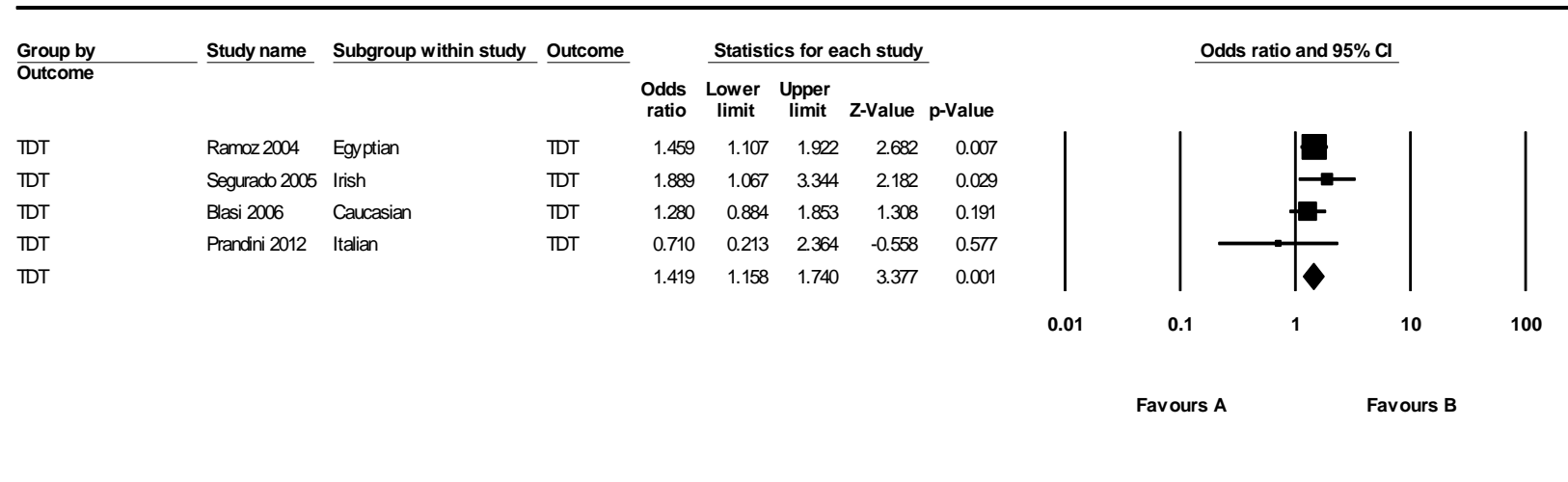
Figure 11: rs2292813 (*SLC25A12*), TDT only

Figure 12: rs2056202 (*SLC25A12*), TDT only

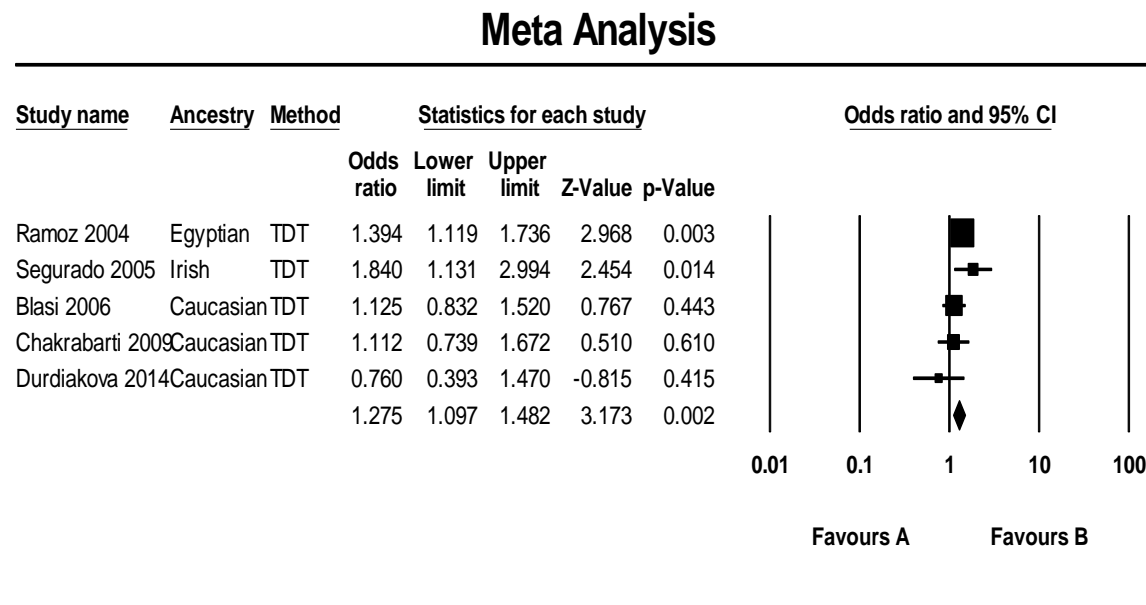


Figure 13: rs1861973 (EN2), TDT only

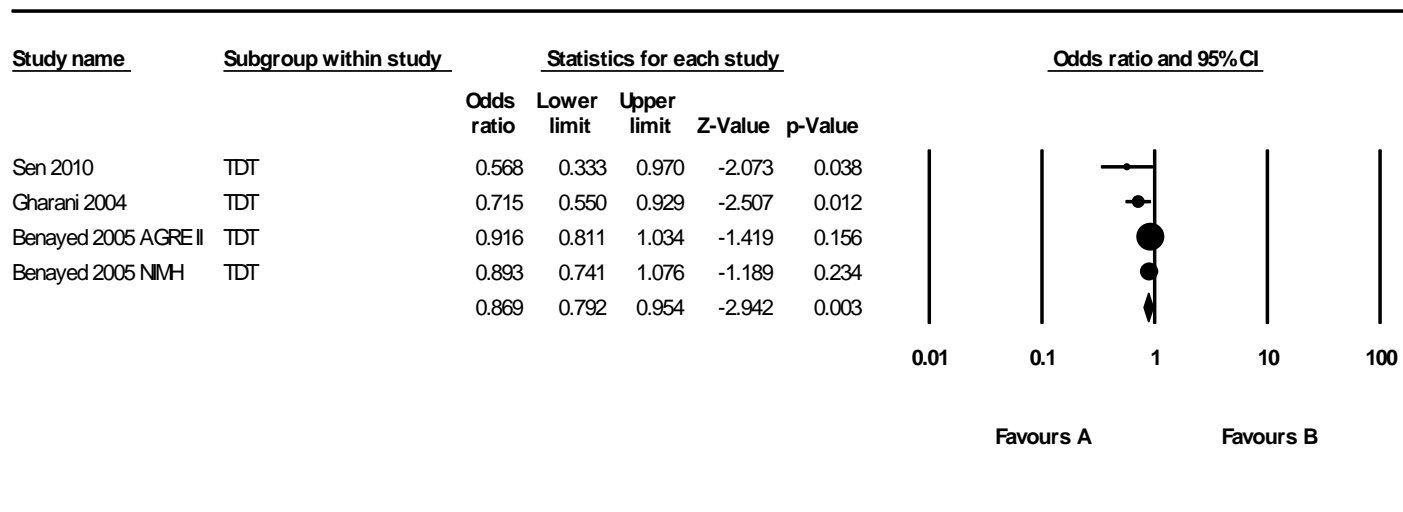


Figure 14: rs1861973 (EN2), Caucasian only

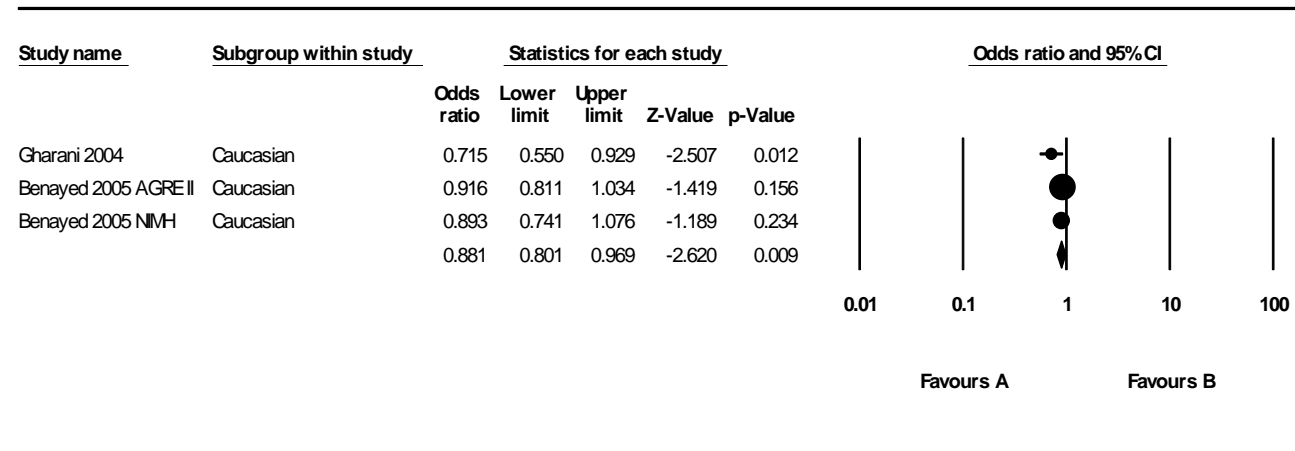
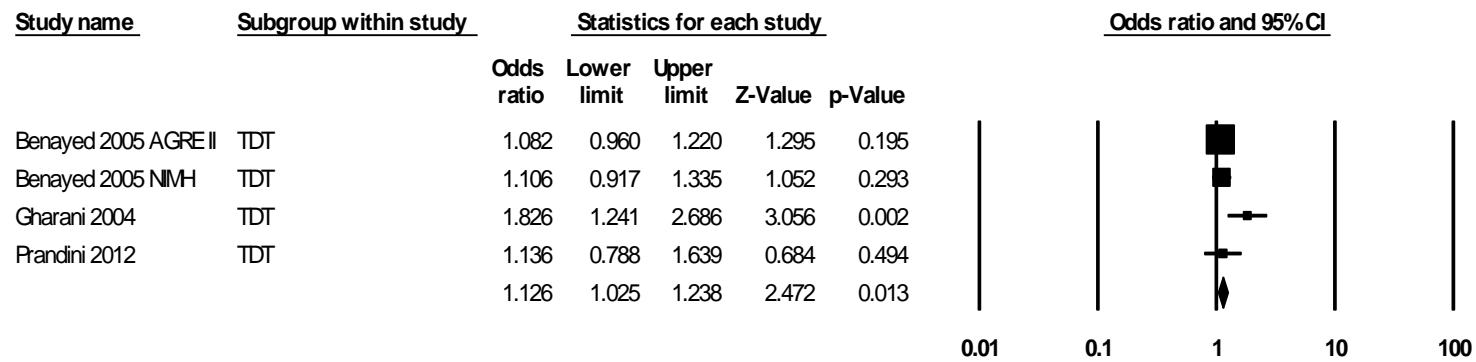


Figure 15: rs1861972 (EN2), TDT only

Meta Analysis



Supplementary Figures 16 – 20: Sensitivity analyses forest plots

Figure 16: Sensitivity analysis for rs4446909 (*ASMT*)

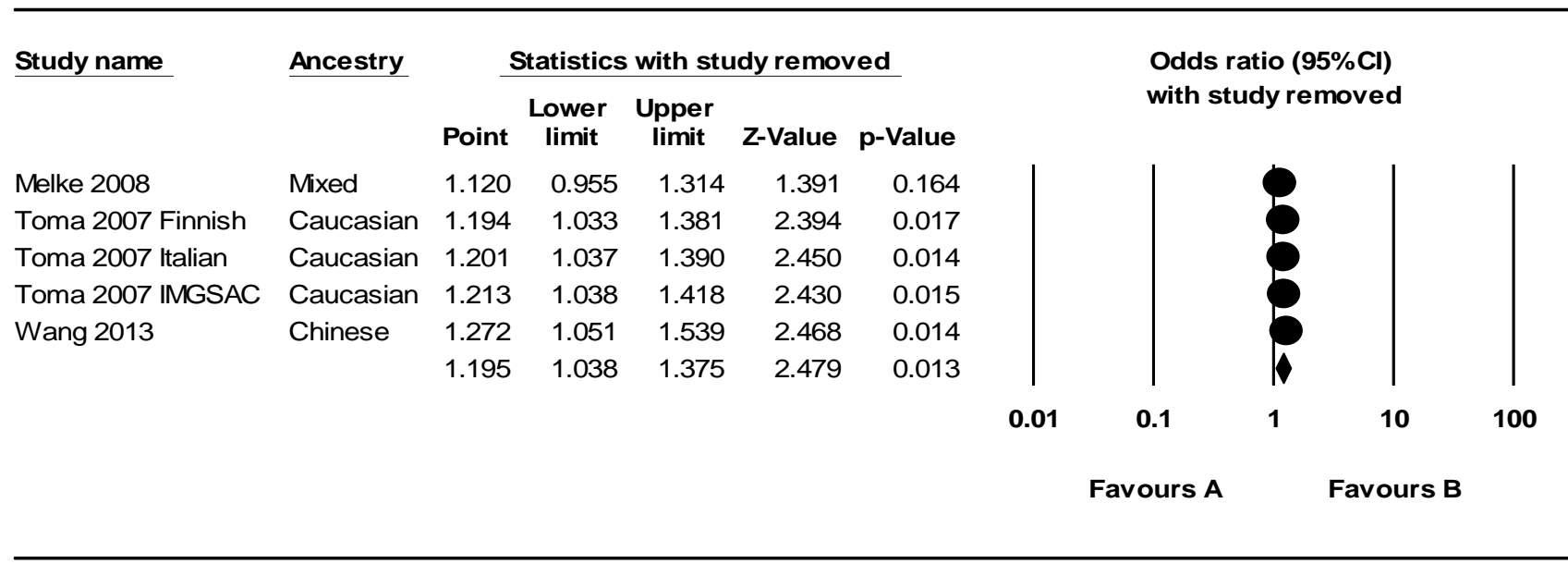


Figure 17: Sensitivity analysis for rs736707 (*RELN*)

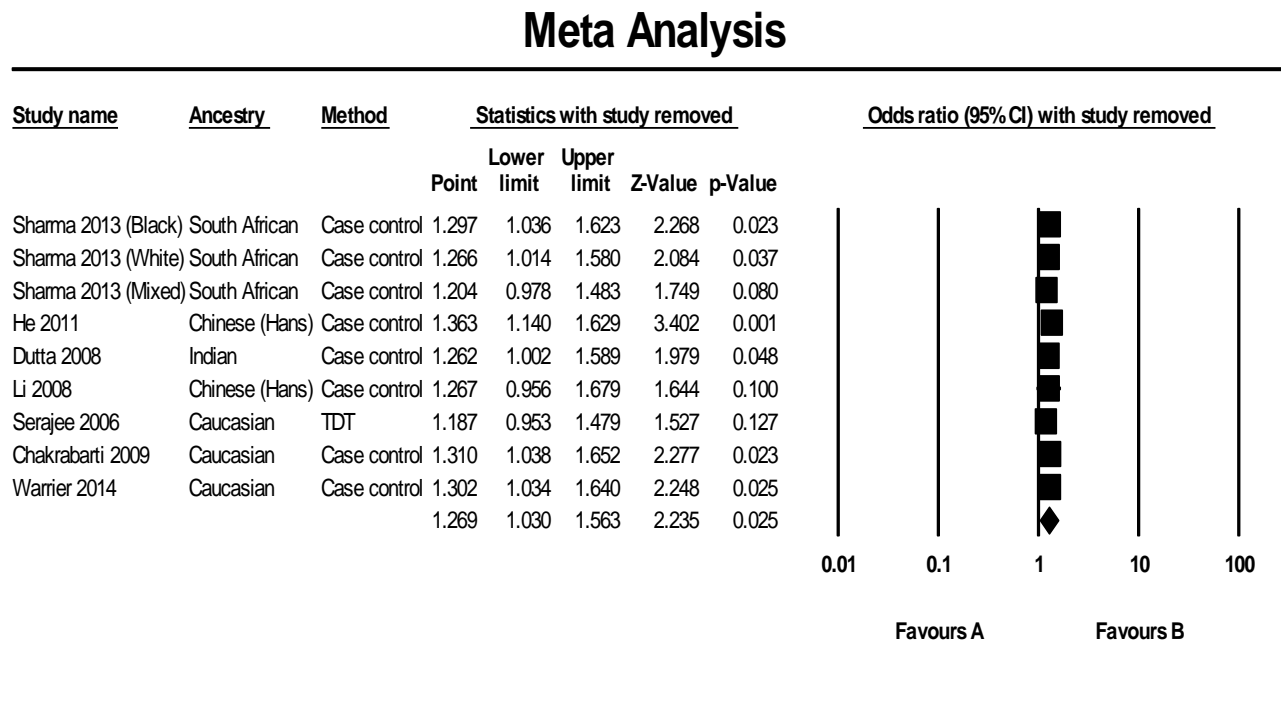


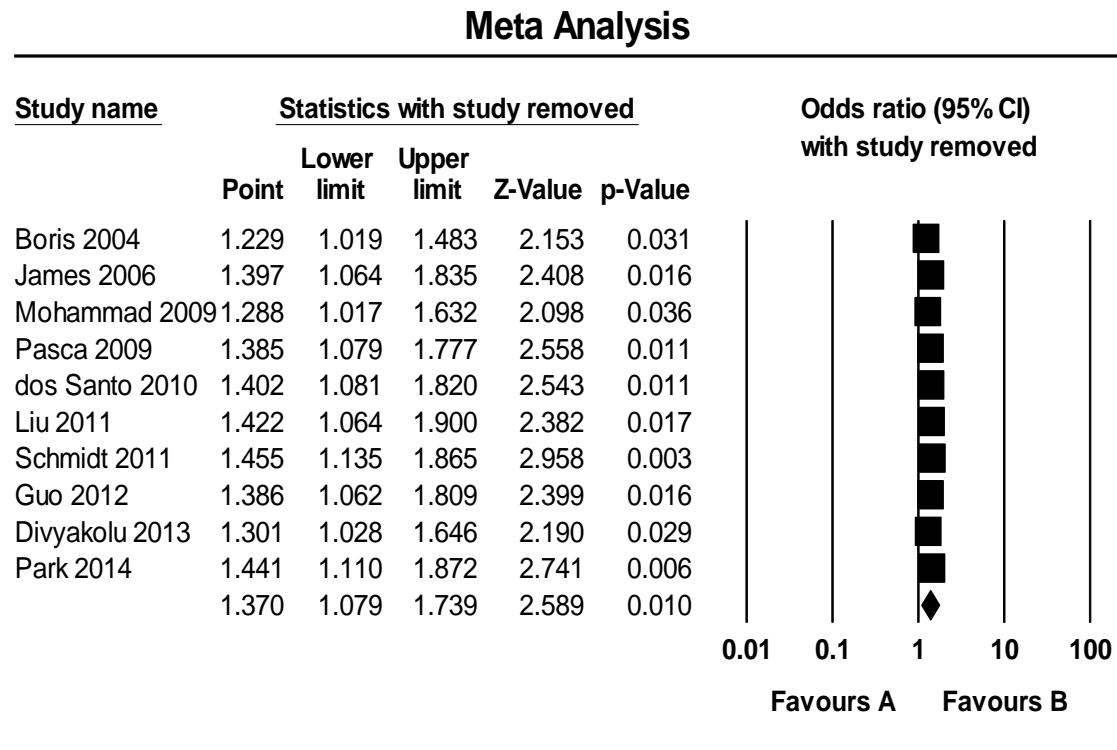
Figure 18: Sensitivity analysis for rs1801133 (*MTHFR*)

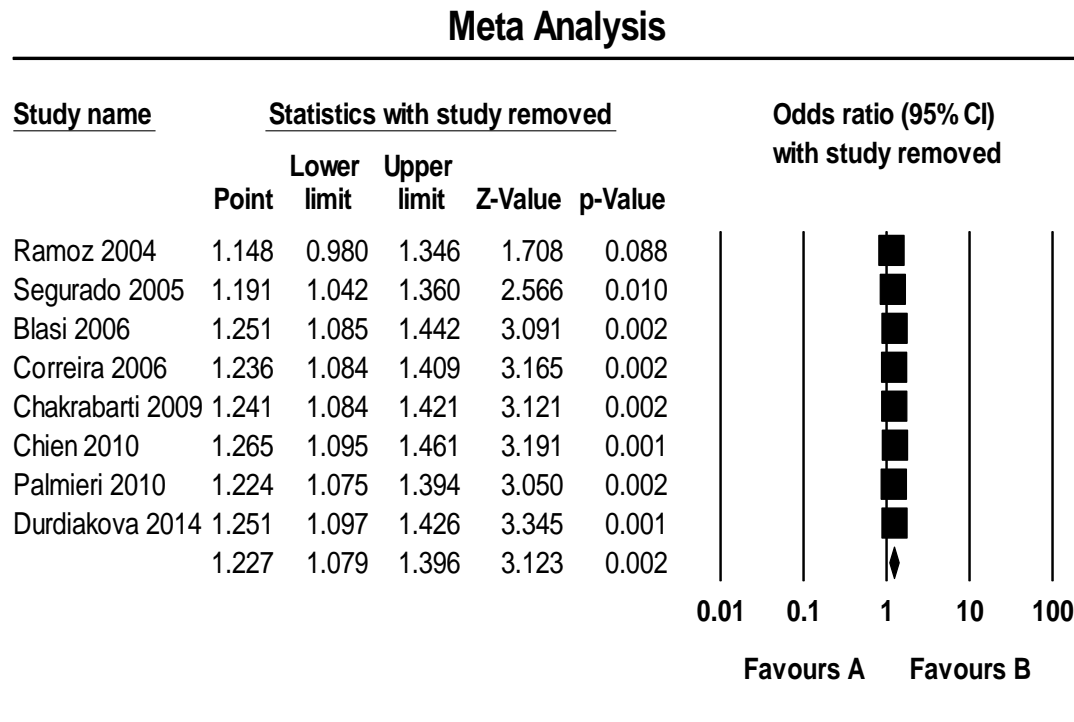
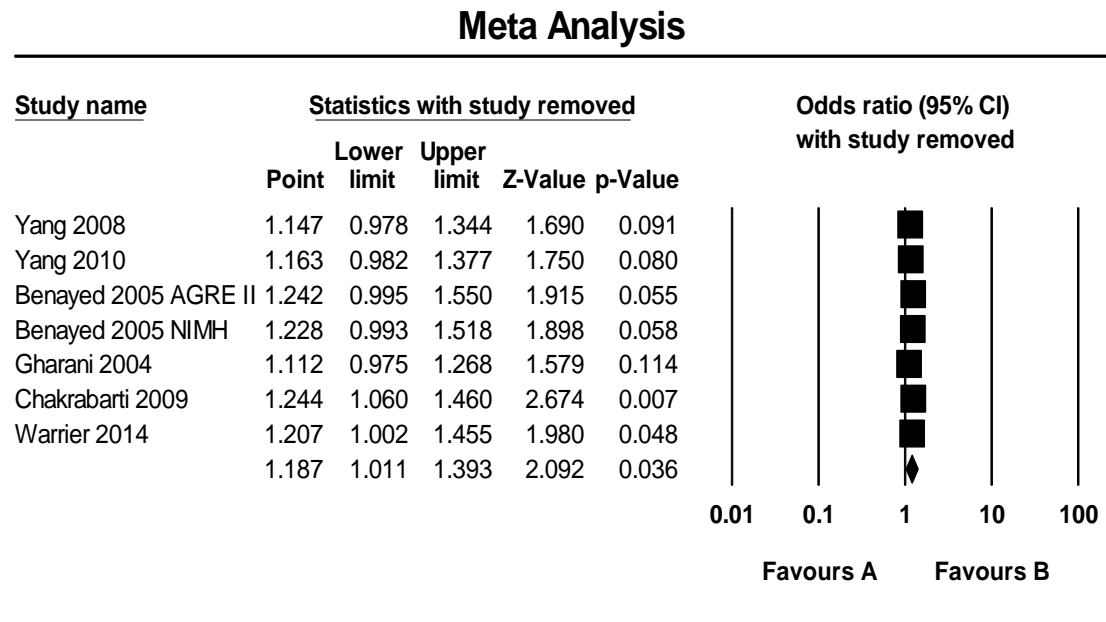
Figure 19: Sensitivity analysis for rs2056202 (*SLC25A12*)

Figure 20: Sensitivity analysis for rs1861972 (EN2)

Details of data from our lab

Cohort 1: Cohort 1 consists of 349 controls (143 males and 206 females) without an ASC diagnosis and were recruited using an advertisement. The mean AQ score for this cohort was 16.43 (range: 3–36, mean score for males: 18.01, mean score for females: 15.33). There were 174 cases (140 males and 34 females). Cases were diagnosed with AS by independent clinicians based on DSM-IV or ICD 10 criteria. The following SNPs used included in the study were genotyped and analysed previously [1]: rs37356353 and rs1861972 in *EN2*; rs6265 in *BDNF*, rs10951145 in *HOXA1*; rs237885 and rs2228485 in *OXTR*. Additionally, for this study, we genotyped the following SNPs: rs4717806 in *STX1A*; rs736707 in *RELN*, rs2056202 in *SLC25A12*; rs53576, rs2254298, rs2268493, rs2268490, rs237894, and rs2301261 in *OXTR*.

Cohort 2: Cohort 2 consists of 118 cases and 412 controls. The controls (185 males, 227 females) had an AQ score below 24. The mean AQ score was 14.9 (range: 2-23, mean score for males: 16.0, mean score for females: 13.9). There were 118 cases (74 males, and 44 females). Cases were diagnosed with AS by independent clinicians based on DSM-IV or ICD 10 criteria. Select SNPs in three genes, namely *OXTR*, *SLC25A12*, *GABRB3*, and *STX1A* were genotyped, analysed and reported previously [2,3,4,5]. SNPs from these genes analysed in this study have been referenced accordingly. In addition, we also genotyped rs1861972 in *EN2* and rs736707 in *RELN*.

All participants reported Caucasian ancestry for at least three generations. DNA was extracted from buccal swabs. Genotyping was performed using TaqMan® SNP genotyping assays, Applied Biosystems Inc., CA. No SNP showed a significant deviation from HWE. Allelic association study was performed using Plink v1.07 [6].

Previous meta-analyses

Five genes investigated in our study have been previously investigated in other meta-analyses. These are: *OXTR*, *RELN*, *HOXA1*, *MTHFR*, and *SLC6A4*. *HOXB1* was previously analysed using meta-analysis and was not re-investigated in our study as there was no new data to include. Our study differs from that of LoParo and Waldman [7], who carried out a meta-analysis of *OXTR* and *ASC*, as they included FBAT studies in their analyses. We excluded studies that used FBAT as FBAT does not report effect sizes. However, we included three additional cohorts, unpublished genotype data from two cohorts from our lab, and a third cohort studied by Nyffeler and colleagues [8]. Of the three variants significant in the previous study, rs237887 and rs2268491 were significant in our study. We did not have enough data to test the third significant variant (rs7632287).

A previous *ASC* and *RELN* meta-analysis [9] investigated three variants (rs736707, rs362691, and the GGC repeat), with only rs362691 giving a statistically significant P-value. In our study, we re-investigated the first two variants using data from additional cohorts. rs736707 was nominally significant and rs362691 was significant in our study. We did not identify any additional data for the GGC repeat and hence did not investigate it in our study. Additionally, we identified a fourth variant in the *RELN* gene, rs2073559, which was not investigated by the previous meta-analysis. This variant was not significant in our study.

We analysed both the variants investigated in a previous meta-analysis [10], of *MTHFR* and *ASC*, including data from two additional studies for rs1801133 and one additional study for rs1801131. The results were similar to the previous results obtained. rs1801133 was significant whereas rs1801131 was not. While the previous study stratified based on folate fortification, we did not conduct these analyses due to insufficient data on folate fortification.

We re-investigated rs10951154 in *HOXA1* which was investigated in an earlier meta-analysis [11]. We included data from the Chakrabarti 2009 cohort in our study, which was not included in the earlier study. While the previous study carried out analyses stratified by ethnicity, they

did not stratify the data based on study methodology, differing from our study. We did not identify any additional data from the *HOXB1* variant, rs72338773, investigated in the previous study [11] and hence did not re-investigate that variant.

Finally, *SLC6A4* has been investigated for ASC using meta-analysis in an earlier study [12]. We extend their work for 5-HTTLPR by using additional data and investigate two additional variants (rs2020936 and rs2020942) in our study. We did not identify any additional data for STin2 VNTR and hence did not re-investigate it.

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